INPLASY PROTOCOL

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None declared.

Efficacy and safety of Chinese herbal medicines in the treatment of allergic rhinitis in children: a systematic review and meta-analysis based on randomized controlled trials

Chen, YH[1]; Wang, J[2]; Wu, LQ[3]; Chen, H[4]; Zhang, ZW[5].

Review question / Objective: **Population: Children (< 18 years) who were definitively diagnosed with allergic rhinitis were included, without concomitant other diseases. No limitation on location or gender. This study will only consider randomized controlled trials (RCTs) of Chinese herbal medicine for treating patients with allergic rhinitis. Other studies, such as animal studies, reviews, case reports, non-controlled studies, and quasi-RCTs, were not included. Comparison: The control intervention is based on allergic rhinitis treatment guidelines or placebo. Outcome: Primary outcomes: Nasal itching, TNSS, or VAS scores. Secondary outcomes: Effective rates, Serum immunoglobulin E (IgE) level, Serum interleukin (IL - 4, IL - 10, IL - 33) levels, Recurrence rate, and Adverse effects. Study design: This meta-analysis is a secondary study, and the data were extracted from other people's work.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 April 2023 and was last updated on 21 April 2023 (registration number INPLASY202340076).

INTRODUCTION

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Condition being studied: Allergic rhinitis is a common respiratory allergic disease in children, mediated by immunoglobulin E. The incidence of allergic rhinitis in children is high, approximately 40 percent, increasing gradually. The incidence of allergic rhinitis in children in China is about 18.61%. Nasal itching, nasal obstruction, runny nose, and sneezing are the main symptoms of allergic rhinitis. Because of the holistic nature of the allergic disease, allergic rhinitis is also related to other conditions, such as asthma, upper airway cough syndrome, and cough-variant asthma. Allergic rhinitis may also affect neurologic development in children, such as those associated with ADHD and multiple tics in children. Therefore, how to control allergic rhinitis is one of the focuses of pediatric research.

Commonly used drugs for allergic rhinitis include glucocorticoids, leukotriene receptor antagonists, antihistamines, and immunotherapy. These therapeutic agents have associated side effects, such as hindering height development, epistaxis, mental excitement, and drowsiness. These inhibit the standard treatment of allergic rhinitis in children. Recurrent allergic rhinitis episodes can affect children's physical and intellectual development. Children are at an essential stage of physical and mental growth and need stable control of the symptoms of allergic rhinitis. Therefore, it is necessary to seek other pharmacological therapies.

Chinese herbal remedies are essential to complementary and alternative medicine and have been used in China for thousands of years. Oral and topical use of Chinese herbal medicines can relieve the nasal symptoms of allergic rhinitis. Chinese herbal therapy can improve inflammatory factors and regulate immune function somewhat. Although studies have shown the therapeutic effect of Chinese herbal remedies in children with allergic rhinitis, there is an insufficient meta-analysis of the role of Chinese herbal medicines in controlling nasal symptoms of allergic rhinitis in children. Therefore, this review and meta-analysis aimed to gather evidence to assess the overall therapeutic role of Chinese herbal medicines for allergic rhinitis in children.

METHODS

Search strategy:

PubMed search strategy

#1 "Drugs, Chinese Herbal"[Mesh]

#2 (((((Chinese Drugs, Plant[Title/Abstract]) OR (Chinese Herbal Drugs[Title/Abstract])) OR (Herbal Drugs, Chinese[Title/Abstract])) OR (Plant Extracts, Chinese[Title/Abstract])) OR (Chinese Plant Extracts[Title/Abstract])) OR (Extracts, Chinese Plant[Title/Abstract])

#3 1# and 2#

#4 "Rhinitis, Allergic"[Mesh]

#5 ((Allergic Rhinitides[Title/Abstract]) OR (Rhinitides, Allergic[Title/Abstract])) OR (Allergic Rhinitis[Title/Abstract])

#6 4 and 5

#7 "Randomized Controlled Trials as Topic"[Mesh]

#8 ((Clinical Trials, Randomized[Title/Abstract]) OR (Trials, Randomized Clinical[Title/Abstract])) OR (Controlled Clinical Trials, Randomized[Title/Abstract])

#9 7 and 8

#10 "Child"[Mesh]

#11 ("Child"[Mesh]) OR (Children[Title/Abstract])

#12 3# and 6# and 9# and 11#

We searched eight databases and one clinical trial registration website. All database retrieval dates are from database establishment to March 2023. The retrieved databases include PubMed, Embase, The Cochrane Library, Web of Science, China National Knowledge Infrastructure, Wanfang Data, CQVIP, Chinese Biological Medicine, and Clinical Trials. gov. Using medical keywords combined with free words for literature search, the main search terms include Chinese herbal

medicine, traditional Chinese medicine, allergic rhinitis, children, and random.

Participant or population: Children (< 18 years) who were definitively diagnosed with allergic rhinitis were included, without concomitant other diseases. No limitation on location or gender.Children (< 18 years) diagnosed with allergic rhinitis, exclude other conditions. No limitation of location or gender.

Intervention: Chinese herbal medicine.

Comparator: The control intervention is based on allergic rhinitis treatment guidelines, or placebo.

Study designs to be included: Random controlled trials of Chinese Herbal Medicine for the treatment of children with allergic rhinitis. The other types of studies will be excluded such as animal studies, reviews, adult studies, case reports, non-controlled trials, and quasi-RCTs.

Eligibility criteria: Inclusion criteria of this study are as follows: 1) Subjects: children with allergic rhinitis diagnosed according to the diagnostic criteria of the Pediatric Branch of the Chinese Medical Association or any other diagnostic criteria with clear consensus, whose age is less than 18 years old, regardless of race and gender; 2) Research type: randomized controlled trials; 3) Intervention method: The experimental group received treatment with Chinese herbal medicine, including alone or in combination with Western medicine, while the control group received treatment with Western medicine or placebo, without limiting the type, usage, and duration of Chinese herbal medicine; 4) Outcome measures: The primary outcome measures include nasal itching score and nasal symptom score, while the secondary outcome measures include response rate, serum IgE level, serum IL-4 level, IL-10 level, IL-33 level, recurrence rate, and adverse events. The exclusion criteria for this study were: 1) acupuncture, massage, or other non-herbal treatments in the experimental group, and the control group received traditional Chinese medicine treatment; 2) In addition to allergic rhinitis, it is accompanied by other diseases; 3) Nasal symptoms were not assessed using TNSS or VAS. Two independent investigators (CYH and WJ) were selected for the study, and a third investigator (WLQ) assessed and resolved all differences between the two researchers and made a final decision.

Information sources: Pubmed, Embase, The Cochrane Library, Web of Science, China National Knowledge Infrastructure, Wanfang Data, CQVIP, Chinese Biological Medicine, and Clinical Trials.gov.

Main outcome(s): Nasal itching score, TNSS score, or VAS score.

Additional outcome(s): Effective rates, Serum immunoglobulin E (IgE) level, Serum interleukin (IL - 4, IL - 10, IL - 33) levels, Recurrence rate, and Adverse effects.

Data management: After retrieving articles, use Endnote 20 software to manage and remove duplicate documents. Two reviewers independently screened titles and abstracts against inclusion and exclusion criteria and then screened full texts for final screening. Two reviewers independently extracted data such as author names, year of publication, basic information about studies, intervention methods, results, and adverse effects using predefined data collection forms and then cross-checked. Unclear data were clarified by the reviewer by e-mail with the study authors. We will use Excel software and Endnote 20 software to manage our data.

Quality assessment / Risk of bias analysis: Two reviewers will separately evaluate the selected RCTs' bias risk using the Cochrane risk of bias assessment tools ROB2.0. The evaluation of each study mainly included six dimensions: random isolation process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of the reported result, and overall bias. Finally, the bias of the study will be rated on three levels: "low", "high", and "some concerns".

Two reviewers will make the assessment separately, and the third will address the discrepancies.

Strategy of data synthesis: This study statistically analyzed the data using Review Manager 5.3 software and StataSE 12 software. The quality of the evidence was summarised and graded using the GRADE methodology and summarized using the GRADE profiler 3.6 software. Dichotomous data were analyzed using risk ratios(RR) with 95% confidence intervals(CI). Continuous data were analyzed using mean difference(MD) or standard mean difference(SMD) with 95% confidence intervals. If the data were homogeneous, a fixed-effect model was used for analysis, whereas a random-effects model was used for analysis. For studies with ten or more references, funnel plots and Egger's test were used to assess publication bias.

Subgroup analysis: The heterogeneity source will be investigated using subgroup analysis based on different interventions.

Sensitivity analysis: The robustness and stability of outcome results will be analyzed by removing low methodological quality studies. The primary analysis point is the impact of method quality, sample size, and missing data on the study. We will assess the effects of individual studies on the overall results to judge whether the results are strong.

Country(ies) involved: China.

Keywords: Chinese Herbal Medicine, Child, Allergic Rhinitis, systematic review, meta-analysis.

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